WEST Search History

DATE: Saturday, September 14, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=AND		
L1	(isoform or iso-form or glycoform or glyco-form)	7133	L1
L2	(premenopaus$ or pre-menopaus$ or post-menopaus$ or postmenopaus$ or menopaus$)	5165	L2
L3	L2 same l1	15	L3
L4	l1.ti and l2.clm.	0	L4
L5	l1.ti,ab,clm. and l2.clm.	1	L5

END OF SEARCH HISTORY

WEST Search History

DATE: Saturday, September 14, 2002

Set Name sid	Query by side	Hit Count	Set Name result s t
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=AND		
L1	(isoform or iso-form or glycoform or glyco-form)	7133	L1
L2	(premenopaus$ or pre-menopaus$ or post-menopaus$ or postmenopaus$ or menopaus$)	5165	L2
L3	L2 same l1	15	L3
L4	l1.ti and l2.clm.	0	L4
L5	l1.ti,ab,clm. and l2.clm.	1	L5
L6	l1 and l2 not l3	197	L6
L7	l6 and (hybridoma or monoclonal or mab or moab or mono-clonal)	123	L7
L8	l1 same (hybridoma or monoclonal or mab or moab or mono-clonal)	561	L8
L9	L8 and l2	10	L9
L10	L9	10	L10

END OF SEARCH HISTORY

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L3: Entry 3 of 15 File: PGPB Apr 18, 2002

DOCUMENT-IDENTIFIER: US 20020045273 A1
TITLE: Test methods and devices

Summary of Invention Paragraph (4):
[0002] Tests are available, or have been proposed, which purport to provide clinically significant information about hormonal levels of relevance to the menopause. The principal hormone of interest is follicle stimulating hormone (FSH). The post-menopausal state has been associated with a rise in the level of circulating FSH. For this purpose tests have been developed to detect the level of FSH in body fluid samples such as blood and urine. These tests are intended to detect "total" FSH, in the sense that they do not discriminate between different isoforms of FSH.

Summary of Invention Paragraph (6):
[0004] Although it is known that FSH exists in various forms, the clinical significance of these in relation to conditions such as the menopause is poorly understood. The differing forms may be isoforms or glycoforms. However, the existence of these differing forms calls into question the soundness of "total" FSH tests as a basis for good clinical diagnosis.

Summary of Invention Paragraph (28):
[0025] Although FSH is the preferred analyte for use in accordance with the invention, other members of the gonadotrophin family can be used. These include human chorionic gonadotrophin (hCG), luteinizing hormone (LH) and thyroid stimulating hormone (TSH). All of these gonadotrophins are glycopeptides. Their principal structure comprises two peptide chains. One peptide chain, known as the alpha chain, is common to all members of the family. The other peptide change, known as the beta chain, differs in each molecule. In addition, each molecule contains glycoprotein side chains. The detailed structure of these molecules is not completely understood. However it is believed that variations in the composition of the glycoprotein side chains give rise to different forms ("glycoforms") of each molecule. Those skilled in the art will appreciate that differences in the chemical properties of the glycoprotein side chains may also influence the physical properties (e.g. charge) of the overall molecule, such that different glycoforms may also constitute different isoforms. Thus, in the case of FSH for example, on present scientific knowledge it is believed that the alpha and beta peptide chains are the same in all FSH forms, but subtle differences occur in the glycoprotein side chains. It is believed that the relative proportions of the forms of FSH existing in the menopause state are different from those in the pre-menopause state.

WEST

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L3: Entry 4 of 15 File: PGPB Apr 11, 2002

DOCUMENT-IDENTIFIER: US 20020042149 A1
TITLE: Test methods and devices

Summary of Invention Paragraph (4):
[0002] Tests are available, or have been proposed, which purport to provide clinically significant information about hormonal levels of relevance to the menopause. The principal hormone of interest is follicle stimulating hormone (FSH). The post-menopausal state has been associated with a rise in the level of circulating FSH. For this purpose tests have been developed to detect the level of FSH in body fluid samples such as blood and urine. These tests are intended to detect "total" FSH, in the sense that they do not discriminate between different isoforms of FSH.

Summary of Invention Paragraph (6):
[0004] Although it is known that FSH exists in various forms, the clinical significance of these in relation to conditions such as the menopause is poorly understood. The differing forms may be isoforms or glycoforms. However, the existence of these differing forms calls into question the soundness of "total" FSH tests as a basis for good clinical diagnosis.

Summary of Invention Paragraph (24):
[0022] Although FSH is the preferred analyte for use in accordance with the invention, other members of the gonadotrophin family can be used. These include human chorionic gonadotrophin (hCG), luteinizing hormone (LH) and thyroid stimulating hormone (TSH). All of these gonadotrophins are glycopeptides. Their principal structure comprises two peptide chains. One peptide chain, known as the alpha chain, is common to all members of the family. The other peptide change, known as the beta chain, differs in each molecule. In addition, each molecule contains glycoprotein side chains. The detailed structure of these molecules is not completely understood. However it is believed that variations in the composition of the glycoprotein side chains give rise to different forms ("glycoforms") of each molecule. Those skilled in the art will appreciate that differences in the chemical properties of the glycoprotein side chains may also influence the physical properties (e.g. charge) of the overall molecule, such that different glycoforms may also constitute different isoforms. Thus, in the case of FSH for example, on present scientific knowledge it is believed that the alpha and beta peptide chains are the same in all FSH forms, but subtle differences occur in the glycoprotein side chains. It is believed that the relative proportions of the forms of FSH existing in the menopause state are different from those in the pre-menopause state.

WEST

Generate Collection | Print

L3: Entry 7 of 15 File: USPT Jul 27, 1999

DOCUMENT-IDENTIFIER: US 5928942 A
TITLE: Hormone-secreting cells derived from pancreatic islet maintained in long-term culture

Brief Summary Text (16):
There exists a need for methods to produce consistent physiologically correct preparations of gonadotrophin hormones. Human gonadotrophin preparations (hMG), which typically contain both FSH and LH, are administered to women who are undergoing pre-treatment leading to in vitro fertilization. The administered hMG stimulates the woman's ovaries to produce multiple pre-ovulatory follicles, which are subsequently aspirated for in vitro fertilization. hMG is currently derived from the urine of post-menopausal women. Each lot differs according to the age and endocrine status of the urine donors, the differences being in both concentration and types of isoforms present in the final product. There are at least 11 isoforms of human follicle-stimulating hormone (hFSH) and 7 isoforms of human luteinizing hormone (hLH) (Stone, B. A., et al. 1990 Acta Endo (Copenhagen) 123: 161-168). Analysis by high-performance liquid chromatography (HPLC) of various hMG preparations showed between-lot variability in the presence and concentration of isoforms of FSH (Stone, B. A. et al, supra). Different isoforms have different biopotencies (Gharib, S. D., et al. 1990 In: Endocrine Reviews 11: 177-199). Since certain isoforms of FSH are more biopotent than others, there is between-lot variability in biopotency among various hMG preparations. Moreover, the presence of LH isoforms in a preparation affects the biopotency of FSH present in the preparation.

Brief Summary Text (21):
There also exists a need for a source of physiologically correct preparations of human sex steroid hormones. Currently, therapeutic estrogen and progesterone compounds, and analogs thereof, are prepared by standardized chemical synthesis. However, the class of compounds designated "estrogens" produced normally in the human female includes several different formulae and isoforms. Similarly, the class of hormones designated "progestins" includes several different compounds and isoforms. The types and amounts of estrogens and progestins produced naturally vary according to the female's age and overall physiological status, i.e., the specific time point in her menstrual cycle, pregnancy, or menopause. The optimal steroid content for any given therapeutic indication has not been determined. Even if the optimal chemical profile of a sex steroid preparation were determined, chemical synthesis would not be a practical route for production of complex steroid mixtures. Therefore, it is desirable to develop methods which inherently provide a physiologically correct mix of human estrogens and progesterones.

WEST

Generate Collection | Print

L3: Entry 11 of 15 File: USPT Nov 16, 1993

DOCUMENT-IDENTIFIER: US 5262518 A
TITLE: Ovulation kit comprising FSH isoforms with varying half-lives

Brief Summary Text (14):
Analysis of the FSH isoforms present within commercial preparations of Pergonal has revealed the domination by the more heavily sialylated (more acidic) forms (Harlin et al., Fert. Steril. 46:1055 (1986); Chappel et al., Acta Endocrinol. 113:311 (1986)). This confirms expectations since the Pergonal preparation is derived from the urine of post-menopausal women. The pituitary gland is known to respond to low circulating levels of estradiol by producing more heavily glycosylated molecules that will survive longer in circulation (Wide and Hobson, J. Clin. Endocrinol. Metabol. 56:371 (1983)). Further, the urine would be expected to accumulate only the FSH forms that are able to survive multiple passes through the liver and kidneys and not be removed by the asialoglycoprotein receptor. The end result is that the FSH present within this commercial preparation exhibits a very prolonged serum half-life.

Brief Summary Text (18):
When women are treated with exogenous gonadotropins prepared from the urine of post-menopausal women, they receive continuous exposure to a very long-acting isoform of FSH. Thus, the selection process to produce a single egg is not efficient, and a large number of follicles are able to survive. Since the FSH molecule produced in post-menopausal women (with low circulating levels of gonadal hormones) is predominantly the heavily sialylated form, repeated injection of long-acting FSH allow follicles to survive that ordinarily would not. Thus, the ovary can become overstimulated which may result in multiple ovulations and perhaps births. Ovarian hyperstimulation may also cause discomfort, ascites and cardiovascular complications.

Brief Summary Text (20):
While more basic and less heavily sialylated forms of FSH might accomplish this, such are not readily available. Because of the presence of infectious agents in human pituitary extracts, that source of basic FSH isoforms also is unavailable. The only other source, extracts of urine obtained from post-menopausal women, contains very low proportions of the basic forms. Thus, until now it has been impossible to provide a physiologic stimulus to women with preparations heretofore available.

Brief Summary Text (24):
Briefly, cDNAs that encode the human alpha and FSH beta subunits are ideally cloned into separate bovine papilloma virus based expression vectors. The mouse metallothionein gene promoter and poly A sequences are provided by the SV40 virus cDNA. Cotransfection of these expression vectors into suitable mammalian cells such as, for example, mouse epithelioid cells (C127) results in the production by such recombinant cells of human FSH that exhibits co- and post-translational modification that is strikingly similar to that observed of FSH found within the anterior pituitary gland. When FSH produced by genetically engineered cells is

separated by the technique of isoelectric focusing, all of the isoforms observed within a normal adult pituitary are observed. This is in striking contrast to the isoelectric focusing profile of FSH present within extracts of urine obtained from post-menopausal females which exhibits preponderance of acidic isoforms. These separated isoforms of FSH are then selectively administered such that the more acid and heavily sialylated forms are given initially and during the therapeutic regimen are gradually changed to smaller quantities of the more basic and lesser sialylated forms. Thus, the most preferred therapeutic compositions of the present invention will comprise recombinant FSH characterized by relatively longer half-life, more sialylation and more acidic isoelectric points, followed by one or more step increments by compositions comprising recombinant FSH characterized by relatively shorter half-life, less sialylation and a more alkaline isoelectric point.

Record Date Created: 19960307

8/9/11
DIALOG(R)File 155:MEDLINE(R)

08604100 95363370 PMID: 7636437

Differences in carbohydrate composition of FSH preparations detected with lectin-ELISA systems.

Rafferty B; Mower J A; Ward H L; Rose M

Division of Endocrinology, National Institute for Biological Standards and Control, South Mimms, Potters Bar, Hertfordshire, UK.

Journal of endocrinology (ENGLAND) Jun 1995, 145 (3) p527-33, ISSN 0022-0795 Journal Code: 0375363

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

FSH is a glycoprotein containing N-linked carbohydrates which exhibit a variety of forms ranging from mono- to multibranched structures. Variation in glycosylation, particularly the degree of terminal sialylation, determines the half-life of the **hormone** and hence its in vivo bioactivity. The **glycoform** content of **FSH** preparations can differ according to the source (e.g. pituitary, urine), cell line (for rDNA-derived material) and selectivity of purification procedures, and may create difficulties in the preparation and characterization of standards and therapeutic products. In order to develop a simple method to detect changes in glycocomposition, an **FSH** ELISA was modified by the incorporation of lectins of recognized sugar specificity, and used to examine the terminal sugar composition of ampouled preparations of pituitary, urinary and rDNA-derived **FSH** . **FSH** was captured with a specific **monoclonal** antibody (**MAb**) and detected with either biotinylated anti- **FSH** **MAb** (ELISA) or the sugar-specific lectins (L-ELISA) from Triticum vulgaris (sialic acid, SA), Sambucus nigra (alpha 2,6-linked SA), Maackia amurensis (alpha 2,3-linked SA) or Ricinus communis (free terminal galactose; GAL). Relative estimates of the amounts of terminal SA, its different forms and GAL were derived from the L-ELISA/ELISA data compared with the highly sialylated 1st International Standard for pituitary FSH (IS) 83/575. All the FSH preparations had less SA than the IS with the ratio of alpha 2,3- and alpha 2,6-linked SA varying between preparations. The amounts of alpha 2,6-linked SA relative to the IS were not significantly different in the urinary and pituitary preparations whereas alpha 2,3-linked SA in all preparations was generally less than that of the standard. (ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Human

Descriptors: *Carbohydrates--analysis--AN; *Follicle Stimulating Hormone --chemistry--CH; Carbohydrate Conformation; Castor Bean; Enzyme-Linked Immunosorbent Assay--methods--MT; Galactose--analysis--AN; Lectins; Phytohemagglutinins; Plants, Toxic; Sialic Acids--analysis--AN; Wheat Germ Agglutinins

CAS Registry No.: 0 (Carbohydrates); 0 (Lectins); 0 (Phytohemagglutinins); 0 (Sambucus nigra lectins); 0 (Sialic Acids); 0 (Wheat Germ Agglutinins); 0 (leukoagglutinins, plants); 0 (ricinus agglutinin); 26566-61-0 (Galactose); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19950913

Development, validation and application of a two-site enzyme-linked immunosorbent assay for activin-AB.

Evans L W; Muttukrishna S; Knight P G; Groome N P

School of Biological and Molecular Sciences, Oxford Brookes University, UK.

Journal of endocrinology (ENGLAND) May 1997, 153 (2) p221-30, ISSN 0022-0795 Journal Code: 0375363

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Monoclonal antibodies, specific for the beta A and beta B subunits of activin, were used to develop a new two-site ELISA for activin-AB. The assay had a detection limit of 0.19 ng/ml. High concentrations of activin-AB were found in bovine, ovine and porcine follicular fluids (FF), with less in human FF (1310, 1730, 688 and 7 ng/ml respectively). Recovery of spiked activin-AB standard from human, bovine and ovine FFs and from homogenized human placental extracts averaged 91%, 115%, 115% and 94% respectively. Within-plate coefficients of variation for different concentration of activin-AB were between 1.3% and 2.67%. The between-plate coefficient of variation was 5.5%. Cross-reactivity experiments showed the high specificity of the assay for activin-AB, with inhibin-A, inhibin-B, follistatin, activin-A and activin-B all cross-reacting < 0.2%. Incubation with high concentrations of follistatin (500 ng/ml) prior to assay did not affect the recovery of activin-AB. Samples of bovine, porcine, ovine and human FF gave dose responses parallel to that of the standard, as did bovine granulosa cell-conditioned media. In human and porcine FF, levels of activin-A and activin-AB were similar whereas, in bovine and ovine FF, activin-A levels were approximately threefold higher than activin-A, nearly all of the endogenous activin-AB in bovine FF was detected in the eluate from gel permeation chromatography with an M(r) of > 700000 indicating its association with higher molecular weight binding protein(s). By contrast, after denaturation, immunoreactive activin-AB was detected with an M(r) of approximately 25000 consistent with the complete dissociation from binding proteins. Activin-A was detected in relatively high concentrations in human FF (approximately 5 ng/ml), homogenized placental extracts (4.35-95.5 ng/g), sera from pregnant women (> 4 ng/ml) and amniotic fluid (3-13 ng/ml), and in much lower concentrations in **postmenopausal** serum (500 pg/ml), normal cycle serum (100-200 pg/ml), serum from **gonadotrophin** -treated women (200 pg/ml), and normal adult male serum (225 pg/ml). Activin-A was also found in the culture media from explants of human amnion, chorion, maternal decidua and placenta. In marked contrast, activin-AB was undetectable (< 0.19 ng/ml) in all of these samples with the exception of human FF (approximately 7 ng/ml). In conclusion, we have developed a sensitive and specific ELISA to measure total (bound+free) activin-AB. Preliminary results show a more restricted distribution of this **isoform** compared with activin-A. The presence of high levels of both activin-A and activin-AB in FF suggests a function for both isoforms in the developing ovarian follicle.

Tags: Animal; Female; Human; Pregnancy; Support, Non-U.S. Gov't

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Human growth **hormone** (GH) exists in a variety of **isoforms** . In the pituitary, the most abundant **isoform** is 22-kD GH (22 K GH), while other **isoforms** (non-22 K GH) are present in variable amounts. In human plasma, the GH heterogeneity contributes to the wide variability in GH levels measured by different immunoassays. The physiological role of the non-22 K GH **isoforms** is poorly understood, but they may represent a spectrum of agonists or antagonists of the GH receptor. It is possible that increased amounts of non-22 K GH **isoforms** in the circulation contribute to the growth failure observed in some short children and may be involved in the pathophysiology of acromegaly and other unrelated diseases. Currently, there is no method available to evaluate the ratio of non-22 K GH isoforms to total GH in large sets of serum samples. In this report, a novel assay procedure is described in which monomeric and dimeric isoforms of 22 K GH are removed from serum and non-22 K GH isoforms are quantitated. The 22 K GH exclusion assay (22 K GHEA) was established as a screening method to identify conditions in which the ratio of non-22 K GH isoforms to total GH in human blood is altered. A 22 K GH-specific **monoclonal** antibody (MCB) is used for binding to 22 K GH in serum. Magnetic beads coated with rat anti-mouse immunoglobulin G and a magnetic device are used to remove the 22K GH-MCB complexes from serum. The non-22 K GH isoforms are measured by a polyclonal antibody-based immunoradiometric assay (GH-IRMA). The assay procedure was optimized systematically by statistical experimental designs. In serum spiked with monomeric or dimeric 22 K GH, the 22 K GH extraction was efficient at GH levels up to 100 microg/l (range 96.3-100%). The intra- and interassay precision for non-22K GH levels of 3.9 microg/l were 2.6% and 8.7%, respectively, while for levels of 0.6 microg/l, which were very close to the detection limits of the assay, the coefficients were 17.0% and 21.6%, respectively. The percentage of non-22 K GH isoforms determined in serum samples from three different groups of subjects showed clearly distinctive values. The 22 K GHEA is a new method for evaluation of non-22 K GH isoforms in human blood under different physiological and pathophysiological conditions.

Tags: Animal; Female; Human; Male; Support, Non-U.S. Gov't
Descriptors: *Somatropin--blood--BL; Adolescence; Adult; Antibodies, Monoclonal; Antibody Specificity; Evaluation Studies; Isomerism; Middle Age ; Molecular Weight; Rats; Recombinant Proteins; Sensitivity and Specificity ; Somatropin--chemistry--CH; Somatropin--deficiency--DF
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Recombinant Proteins) ; 12629-01-5 (Somatropin)
Record Date Created: 19970204

7/9/14
DIALOG(R)File 155:MEDLINE(R)

09675994 98096847 PMID: 9435121
On-line post-capillary affinity detection of immunoglobulin G subclasses and monoclonal **antibody variants for capillary electrophoresis.**
Kelly J A; Lee C S
Department of Chemistry, Iowa State University, Ames 50011, USA.
Journal of chromatography. A (NETHERLANDS) Nov 28 1997, 790 (1-2) p207-14, Journal Code: 9318488
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Human immunoglobulin G (IgG) subclasses each play a unique role in an immune response to foreign antigens. Three of the human IgG subclasses have distinct electrophoretic mobilities and are resolved by capillary zone electrophoresis (CZE). A post-capillary reactor is constructed to allow on-line addition of fragment B (of protein A)-fluorescein to form affinity complexes with separated IgG subclasses. Post-capillary affinity detection provides selective identification of human IgG subclasses and illustrates the effect of affinity binding constant on detection sensitivity.

Additionally, post-capillary affinity detection for CZE facilitates rapid and selective heterogeneity analysis of mouse **monoclonal** anti-(human-alpha 1-antitrypsin) and anti-human follicle stimulating **hormone** in complex sample matrices. A constant mobility difference is observed between the antibody **isoforms** , likely the result of charge heterogeneity due to deamination, degradation or variation in sialic acid content.

Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: Antibodies, **Monoclonal** --analysis--AN; *Immunoglobulin G --analysis--AN; Chromatography, Affinity; Electrophoresis, Capillary; Fluoresceins; Fluorescent Dyes; Mice; Spectrophotometry, Ultraviolet

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Fluoresceins); 0 (Fluorescent Dyes); 0 (Immunoglobulin G)

Record Date Created: 19980211

7/9/1

DIALOG(R)File 155:MEDLINE(R)

09583641 98007740 PMID: 9349584

Paracrine effect of human chorionic gonadotropin ectopically produced from papillary thyroid cancer cells on growth and function of FRTL-5 rat thyroid cells.

Sakaguchi N; Yoshimura M; Hershman J M; Nishikawa M; Inada M

Second Department of Internal Medicine, Kansai Medical University, Moriguchi, Osaka, Japan.

Thyroid : official journal of the American Thyroid Association (UNITED STATES) Oct 1997, 7 (5) p779-82, ISSN 1050-7256 Journal Code: 9104317

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

It is well known that human chorionic gonadotropin (hCG) is sometimes secreted from nontrophoblastic neoplasms. To elucidate the role of ectopic hCG, we investigated the effect of hCG produced from a papillary thyroid cancer cell line (B-CPAP cells) on stimulation and growth promotion of FRTL-5 rat thyroid cells. Ectopic hCG contained in the culture medium of B-CPAP cells was purified using gel filtration and bioassayed for thyrotropic activity in FRTL-5 cells. Addition of ectopic hCG (up to 5.2 x 10(4) IU/L) increased cyclic adenosine monophosphate (cAMP) accumulation and 3H-thymidine incorporation in FRTL-5 cells dose dependently. These effects were almost as potent as the stimulation induced by standard hCG CR-127. After the absorption of the ectopic hCG by anti-hCG-beta **monoclonal** antibody, the cAMP accumulation was significantly decreased. Analysis of ectopic **hCG** **isoforms** with different isoelectric points indicated the predominance of the acidic **hCG** **isoform** with isoelectric point (pI) 3.8-3.2 that is the major **isoform** of standard **hCG** . Basic **isoforms** (pI 5.7-5.3) with higher thyrotropic potency were also detected. These results indicate that the ectopic **hCG** secreted from papillary thyroid cancer cells possess intrinsic thyroid-stimulating and growth-promoting activity. The ectopic **hCG** may act as an autocrine-paracrine factor in nontrophoblastic neoplasms.

Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Carcinoma, Papillary--secretion--SE; *Gonadotropins, Chorionic--secretion--SE; *Hormones, Ectopic--secretion--SE; *Thyroid Gland --cytology--CY; *Thyroid Neoplasms--secretion--SE; Carcinoma, Papillary --pathology--PA; Cell Division--drug effects--DE; Cell Line; Cyclic AMP --metabolism--ME; Gonadotropins, Chorionic--pharmacology--PD; Hormones, Ectopic--pharmacology--PD; Isoelectric Focusing; Rats; Thyroid Gland--drug effects--DE; Thyroid Gland--metabolism--ME; Thyroid Neoplasms--pathology --PA; Tumor Cells, Cultured

CAS Registry No.: 0 (Gonadotropins, Chorionic); 0 (Hormones, Ectopic) ; 60-92-4 (Cyclic AMP)

Record Date Created: 19971113

7/9/2
DIALOG(R)File 155:MEDLINE(R)

10355078 99320653 PMID: 10392356
Growth hormone isoforms in a girl with gigantism.
Ng L L; Chasalow F I; Escobar O; Blethen S L
Department of Pediatrics, SUNY at Stony Brook, USA.
Journal of pediatric endocrinology & metabolism : JPEM (ENGLAND) Jan-Feb 1999, 12 (1) p99-106, Journal Code: 9508900
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Several previous investigations have suggested that there may be different growth hormone isoforms in patients with acromegaly. We used three different site-specific **monoclonal** antibodies (MAbs) to investigate growth **hormone** (GH) **isoforms** in serum from an 8 year-old girl with a GH and prolactin secreting adenoma. The pattern of GH-immunoreactivity was dependent on the circumstances of collection. Serum obtained after oral glucose had very little cross reactivity with **MAb** 352 although concentrations of up to 15 micrograms/l were found with two other MAbs, 033 and 665. **MAb** 352 does not recognize the 20,000 dalton **isoform** of GH (20K) while both **MAb** 033 and 665 do. The same pattern of GH immunoreactivity (low **MAb** 352, equal and higher **MAb** 033 and 665) was seen in other baseline samples. In contrast, samples obtained after TRH/GnRH showed immunoreactivity patterns expected for a mixture of 22,000 dalton isoform of GH (22K) with only a small amount of 20K. GH samples obtained during sleep showed both patterns with episodic peaks with equal immunoreactivity superimposed on the basal pattern (decreased activity with **MAb** 352). Affinity chromatography of basal samples showed that a portion of the GH immunoreactivity was neither 22K nor 20K, although in stimulated samples, over 70% of GH was 22K or 20K GH. In conclusion, the nature of GH isoforms present in serum varies with GH concentration. These differences may contribute to the known difficulty in correlating disease activity and random GH measurements in patients with GH secreting adenomas.
Tags: Case Report; Female; Human
Descriptors: *Gigantism--blood--BL; *Pituitary Neoplasms--blood--BL; *Prolactinoma--blood--BL; *Somatotropin--blood--BL; Child; Chromatography, Affinity; Circadian Rhythm; Gigantism--diagnosis--DI; Gigantism--etiology --ET; Magnetic Resonance Imaging; Pituitary Neoplasms--complications--CO; Pituitary Neoplasms--diagnosis--DI; Prolactin--blood--BL; Prolactinoma --complications--CO; Prolactinoma--diagnosis--DI; Protein Isoforms--blood --BL; Radioimmunoassay
CAS Registry No.: 0 (Protein Isoforms); 9002-62-4 (Prolactin); 9002-72-6 (Somatotropin)
Record Date Created: 19990920

7/9/4
DIALOG(R)File 155:MEDLINE(R)

09150211 97046607 PMID: 8891528
Glycosylation is the structural basis for changes in polymorphism and immunoreactivity of pituitary glycoprotein hormones.
Zerfaoui M; Ronin C
UPR 9024 CNRS, Marseille, France.
European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p749-53, ISSN 0939-4974 Journal Code: 9105775
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Glycoprotein hormones have long been known to display extensive polymorphism and changes in bioactivity according to the endocrine status of the patient. Structural analysis has shown that pituitary gonadotropins (lutropin and follitropin) and thyrotropin are synthesized and secreted as

a panel of isoforms which differ in glycosylation, bioactivity and circulatory half-life. Ultrasensitive immunoassays could reveal that glycosylation of plasma **hormones** is structurally different from the pituitary stock so that the ratio of circulating **glycoforms** may vary according to the physiopathology of the pituitary axis. However, contradictory results between immunoassays have been often reported, suggesting that some plasma forms can escape recognition by **monoclonal** antibodies which have been raised to the pituitary or urinary antigen. When **hormone** levels do not correlate with clinical features, one can also suspect that inactive or hyperactive forms are being measured. At the molecular level, very limited information has been gained toward the expression of **hormone** epitopes as a function of carbohydrate structure. To address this issue, we have compared the recognition of pituitary and recombinant human thyrotropin by various polyclonal and **monoclonal** antibodies before and after neuraminidase treatment. Both, pituitary and recombinant thyrotropin bound to anti-alpha and anti-beta antibodies, demonstrating thereby that recombinant thyrotropin can be used to calibrate immunoassays. While removal of sialic acid did not alter the recognition of the recombinant **hormone** in various immunoassays, this treatment specifically abolished the binding of pituitary thyrotropin to anti-beta **monoclonal** antibodies. These findings show that immunoreactivity of circulating **hormone** **glycoforms** , which are often more sialylated than their pituitary counterparts, may very well account for variation depending on the antibodies used in the immunoassays. (12 Refs.)

Tags: Human

Descriptors: *Pituitary Hormones--chemistry--CH; *Pituitary Hormones --genetics--GE; *Polymorphism (Genetics); Follicle Stimulating Hormone --chemistry--CH; Follicle Stimulating Hormone--genetics--GE; Glycoproteins --chemistry--CH; Glycoproteins--genetics--GE; Glycosylation; Gonadotropins , Chorionic--chemistry--CH; Gonadotropins, Chorionic--genetics--GE; Immunoassay; Isoelectric Focusing; LH--chemistry--CH; LH--genetics--GE; Pituitary Hormones--immunology--IM; Recombinant Proteins--chemistry--CH; Thyrotropin--chemistry--CH; Thyrotropin--genetics--GE

CAS Registry No.: 0 (Glycoproteins); 0 (Gonadotropins, Chorionic); 0 (Pituitary Hormones); 0 (Recombinant Proteins); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone); 9002-71-5 (Thyrotropin)

Record Date Created: 19970206

7/9/5

DIALOG(R)File 155:MEDLINE(R)

09461283 97378697 PMID: 9234300

Heterogeneity of plasma gonadotropins. Consequences on immunological properties of LH.

Roger M; Lalhou N

Hopital Saint-Vincent-de-Paul, Paris, France.

Nuclear medicine and biology (ENGLAND) Apr 1994, 21 (3) p349-57, ISSN 0969-8051 Journal Code: 9304420

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The pituitary gonadotropins **FSH** and **LH** are secreted into blood as dimeric glycoproteins which display a wide heterogeneity when submitted to technique of separation based on electric charge. That supports the assumption of a major role of the carbohydrates moieties as a source of heterogeneity. No clear difference however has been demonstrated in the biological potency of the different **isoforms** occurring in blood. On the contrary, important discrepancies in immunological activity have been evidenced, mainly as far as **LH** is concerned. This is particularly important from a practical point of view since some **monoclonal** sandwich assays widely used for the measurement of **LH** levels fail to detect **LH** in samples from certain subjects. The description of the so-called "invisible **LH** " phenomenon should prompt international organizations to incite the manufacturers of commercial kits to improve the standardization in **gonadotropin** assays. (30 Refs.)

Tags: Female; Human; Male

Descriptors: *Follicle Stimulating Hormone--blood--BL; *LH--blood--BL; Immunoassay; LH--immunology--IM; Protein Conformation
CAS Registry No.: 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19970918

7/9/11
DIALOG(R)File 155:MEDLINE(R)

09038853 96389001 PMID: 8796333
European collaborative study of LH assay: 3. relationship of immunological reactivity, biological activity and charge of human luteinizing hormone.
Niccoli P; Costagliola S; Patricot M C; Mallet B; Benahmed M; Carayon P
Laboratoire de Biochimie Endocrinienne et Metabolique, Unite 38 INSERM, Faculte de Medecine, Marseille, France.
Journal of endocrinological investigation (ITALY) May 1996, 19 (5) p260-7, ISSN 0391-4097 Journal Code: 7806594
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
This report describes the results of the third part of the collaborative study organized by a working group sponsored by the Community Bureau of Reference of the European Community Commission. The aim of the present work was to establish the link between immunoreactivity and biological activity of human LH, thus allowing to determine the antigenic domains of the molecule involved in the induction of the biological effect. The relationship between immunoreactivity and electric charge of hLH was also studied. This work allowed to further apprehend hLH isomorphism and its role in discrepancies observed among hLH assays and clinical status. It also made the feasibility of measuring biologically active isoforms by an immunological method to be assessed. The effect of 36 mAb with known epitopic specificity, was evaluated on both hLH binding to rat membrane receptor and hLH induced production of testosterone by porcine Leydig cells. All the epitopes located on the beta subunit were found to be strongly involved in the biological activity whereas 4/9 and 10/18 epitopes present on the alpha subunit or specific for the holomolecule respectively appeared weakly involved. Assaying biological **hLH** using immunological method would require that mAb specific for all the epitopes involved in the receptor activation be tested, and thus appears presently unsuitable for routine clinical evaluation. In the previous work some **LH** immunoassays were found to underestimate **LH** concentrations (J. Endocrinol. Invest 1994, 17: 397-406 and 407-416). The mAb used in liquid phase in these kits were found in the present work to be directed against the domains of **LH** weakly involved in the activation of the receptor and would suggest that bioactive **LH** would be misevaluated by these kits. The immunoreactivity of **hLH isoforms** separated by isoelectric focusing (IEF) in liquid phase was also determined. IEF allowed to separate three groups of **hLH isoforms** but none of them exhibited a specific discriminating pattern of immunoreactivity when they were tested against a panel of mAb. It suggests that, in our experimental conditions, the electric charge and the immunoreactivity of **hLH** were not closely linked.
Tags: Animal; Human; Male
Descriptors: *LH--immunology--IM; *LH--physiology--PH; Antibodies, Monoclonal--immunology--IM; Antibody Specificity; Cell Membrane--metabolism --ME; Electrochemistry; Epitopes--analysis--AN; Epitopes--immunology--IM; Epitopes--physiology--PH; Immunoassay; Isoelectric Focusing; LH --pharmacology--PD; Leydig Cells--drug effects--DE; Leydig Cells --metabolism--ME; Pituitary Gland--chemistry--CH; Rats; Receptors, LH --metabolism--ME; Swine; Testosterone--biosynthesis--BI
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Receptors, LH); 57-85-2 (Testosterone); 9002-67-9 (LH)
Record Date Created: 19970221

7/9/12

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The impact of the adoption of the new biosynthetic growth hormone (GH) WHO International Reference Preparation (IRP 88/624), and the recommendation to report results in microgram/L instead of mU/L, is described. Conversion factors were determined by comparing both the linear and nonlinear relations of the GH values. The Pharmacia polyclonal IRMA (p-IRMA) and the DELFIA **monoclonal** time-resolved immunofluorometric assay (trIFMA) with kit calibrators calibrated either against the pituitary-derived WHO IRP 80/505 or the new 88/624 were evaluated. Conversion factors of 4.17 mU/L = 1 microgram/L for the p-IRMA and 4.31 mU/L = 1 microgram/L for the trIFMA were necessary. Different cross-reactivity patterns for the deaminated and dimer 22-kDa, 20-kDa, and 17-kDa GH isoforms were found. Expected GH recovery was similar when the measured values were adjusted according to the results of the cross-reactivity study.

Tags: Female; Human; Support, Non-U.S. Gov't

Descriptors: *Carrier Proteins--blood--BL; *Reagent Kits, Diagnostic; *Somatropin--blood--BL; Adolescence; Antibodies; Antibodies, **Monoclonal** ; Child; Fluoroimmunoassay; Isomerism; Reference Standards; World Health Organization

CAS Registry No.: 0 (Antibodies); 0 (Antibodies, Monoclonal); 0 (Carrier Proteins); 0 (Reagent Kits, Diagnostic); 0 (somatotropin-binding protein); 12629-01-5 (Somatropin)

Record Date Created: 19970714

7/9/36

DIALOG(R)File 155:MEDLINE(R)

09329212 97227031 PMID: 9133248

Interassay differences in growth hormone measurement in acromegaly.

Barth J H; Smith J H; Clarkson P

Department of Chemical Pathology and Immunology, Leeds General Infirmary, UK.

Annals of clinical biochemistry (ENGLAND) Mar 1997, 34 (Pt 2) p156-9 , ISSN 0004-5632 Journal Code: 0324055

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

We measured plasma growth **hormone** concentrations by three different two-site immunometric assays (Pharmacia hGH RIA, IDS Gamma-BCT and Delfia 22 kDa hGH) to determine whether there are GH **isoforms** secreted by acromegalic patients that are under-recognized by some assays. There was a fairly good agreement between assays with the IDS Gamma-BCT and Delfia 22 kDa assays giving lower results than the Pharmacia IRMA. GH was measured on stored plasma samples from 24 patients with proven acromegaly. There was a consistent difference between the three assays of approximately 20% of the mean value for each patient.

Tags: Female; Human; Male

Descriptors: *Acromegaly--blood--BL; *Somatropin--blood--BL; Adolescence; Adult; Aged; Antibodies, **Monoclonal** --analysis--AN; Middle Age; Radioimmunoassay; Reproducibility of Results; Somatropin--immunology--IM

CAS Registry No.: 0 (Antibodies, Monoclonal); 12629-01-5 (Somatropin)

Record Date Created: 19970430

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DIALOG(R)File 155:MEDLINE(R)

10124154 99110190 PMID: 9894899

Construction of a specific and sensitive sandwich enzyme immunoassay for 20 kDa human growth hormone.

Hashimoto Y; Ikeda I; Ikeda M; Takahashi Y; Hosaka M; Uchida H; Kono N; Fukui H; Makino T; Honjo M

Institute of Biological Science, Mitsui Pharmaceuticals, Mobara, Chiba, Japan.

Journal of immunological methods (NETHERLANDS) Dec 1 1998, 221 (1-2) p77-85, ISSN 0022-1759 Journal Code: 1305440

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Twenty kilodalton human growth **hormone** (20K-hGH) is a naturally occurring **isoform** lacking amino acid residues 32-46 of 22K-hGH. Due to this structural similarity to 22K-hGH, no one has constructed a specific and sensitive assay system for 20K-hGH, which can be used for measuring physiological concentration of this **isoform** in the circulation. To construct such a specific assay system, we have generated polyclonal antibodies (pAb) and **monoclonal** antibodies (mAbs) against recombinant 20K-hGH. Binding characteristics to 20K-, 22K-hGH and monkey GH (mGH) of these five mAbs, designated A23, B13, C02, D05, and D14, were analyzed by enzyme immunoassays (EIAs) and surface plasmon resonance analysis. Only one of them, the **mAb** D05, does not crossreact with 22K-hGH. It was also observed that **mAb** B13 does not crossreact with mGH, although the later is 96% homologous to hGH. Using these antibodies we have established several sandwich EIA systems for circulating 20K-hGH. The combination of A23 as a solid-phase antibody and B13 as a labeled antibody permitted both high sensitivity to 20K-hGH (< 0.1 ng/ml) and low cross-reactivities with 22K-hGH (< 2%), mGH (< 0.3%) and rat GH (< 0.1%). The clearances of administered 20K-hGH were determined by this combination in both rats and monkeys. In the assay of physiologically circulating 20K-hGH in humans, the combination of D05 and affinity-purified anti-20K-hGH pAb showed the highest sensitivity to 20K-hGH (< 10 pg/ml) and substantially no cross-reactivity with 22K-hGH (< 0.1%). The plasma 20K-hGH concentration in healthy female subjects was determined by this combination. The assay systems constructed here enables us to directly measure circulating 20K-hGH in physiological condition with no interference of 22K-hGH for the first time.

Tags: Animal; Female; Human; Male

Descriptors: Antibodies--metabolism--ME; *Antibodies, **Monoclonal** --biosynthesis--BI; *Immunoenzyme Techniques--methods--MT; *Somatropin --analysis--AN; Adult; Antibodies--blood--BL; Antibodies--immunology--IM; Antibodies, **Monoclonal** --blood--BL; Antibodies, **Monoclonal** --immunology --IM; Antibody Specificity; Epitopes--analysis--AN; Macaca fascicularis; Mice; Mice, Inbred BALB C; Protein Isoforms; Rabbits; Rats; Rats, Sprague-Dawley; Sensitivity and Specificity; Somatotropin--analysis--AN; Somatotropin--blood--BL; Somatotropin--immunology--IM; Somatropin--blood --BL; Somatropin--immunology--IM

CAS Registry No.: 0 (Antibodies); 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Protein Isoforms); 12629-01-5 (Somatropin); 9002-72-6 (Somatotropin)

Record Date Created: 19990129

7/9/28

DIALOG(R)File 155:MEDLINE(R)

09437117 97334879 PMID: 9191545

Growth hormone (GH) assays: influence of standard preparations, GH isoforms , assay characteristics, and GH-binding protein.

Jansson C; Boguszewski C; Rosberg S; Carlsson L; Albertsson-Wikland K

Department of Pediatrics, University of Goteborg, Sweden. chatarina.jansson@pediat.gu.se

Clinical chemistry (UNITED STATES) Jun 1997, 43 (6 Pt 1) p950-6, ISSN 0009-9147 Journal Code: 9421549

8/9/3
DIALOG(R)File 155:MEDLINE(R)

08914922 96263537 PMID: 8785562
Turner's syndrome and isoforms **of** LH **and** FSH **. Value of polyclonal enzymatic techniques]**
Syndrome de Turner et **isoformes** de **LH** et **FSH** . Interet des techniques enzymatiques polyclonales.
Petrus M; Rittie J L; Causse J E; Moulie N; Rhabbour M; Netter J C; Hirsch C; Bildstein G
Service de pediatrie, CHU, Tarbes, France.
Archives de pediatrie : organe officiel de la Societe francaise de pediatrie (FRANCE) Mar 1996, 3 (3) p245-7, ISSN 0929-693X Journal Code: 9421356
Document type: Journal Article ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
BACKGROUND: The glycoproteic **hormones** , **LH** and **FSH** , circulate under heterogenous molecular forms, the **isoforms** . The more acidic **isoforms** of **FSH** are found in hypogonadic patients and a displacement towards the basic forms is observed during substitutive treatment. CASE REPORT: A 13 year-old girl with Turner syndrome was examined for pubertal delay. Ultrasonography failed to see both ovaries and endocrine investigations showed a type P1 response (**LH** -RH test using immunological method). Control of hormonal levels by a polyclonal immunoenzymatic method confirmed primary hypogonadism. CONCLUSIONS: Radioimmunological methods using **monoclonal** antibodies can underevaluate **FSH** and **LH** levels under circumstances in which the distribution of **isoforms** may vary. Discrepancy must lead to the measure of **gonadotrophins** using polyclonal immunoenzymatic methods.
Tags: Case Report; Female; Human
Descriptors: *Follicle Stimulating Hormone--blood--BL; *Follicle Stimulating Hormone--chemistry--CH; *Immunoenzyme Techniques; *LH--blood --BL; *LH--chemistry--CH; *Turner Syndrome--blood--BL; Hypogonadism--blood --BL
CAS Registry No.: 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19960924

8/9/5
DIALOG(R)File 155:MEDLINE(R)

08855017 96186174 PMID: 8636376
Characterization of monoclonal **antibodies specific for the human growth** hormone **22K and 20K** isoforms **.**
Mellado M; Rodriguez-Frade J M; Kremer L; Martinez-Alonso C
Department of Immunology and Oncology, Centro Nacional de Biotecnologia, Campus Cantoblanco, Universidad Autonoma, Madrid, Spain. jmmelladosamba.cnb.uam.es.
Journal of clinical endocrinology and metabolism (UNITED STATES) Apr 1996, 81 (4) p1613-8, ISSN 0021-972X Journal Code: 0375362
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS
We have derived and characterized a set of **monoclonal** antibodies (**mAb**) specific for the different human GH (hGH) isoforms. The binding characteristics of each antibody to the hGH isoforms (22K and 20K) were analyzed in direct and competitive immunoassays as well as by Western blot. We studied the effects of these **mAb** on the biological activity of hGH and showed that they specifically block their respective activities. Using these **mAb** , we developed several immunoassays that have been applied for the quantitation of the different hGH isoforms in body fluids. Therefore, these **mAb** may help to unravel the biological function of these variants.
Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: *Muscle Proteins--biosynthesis--BI; *Somatotropin--analysis --AN; Antibodies, **Monoclonal** ; Antibody Specificity; Blotting, Western --methods--MT; Body Fluids--chemistry--CH; Immunoenzyme Techniques; Mice; Mice, Inbred BALB C; Mice, Inbred C3H; Mice, Inbred C57BL; Radioimmunoassay --methods--MT; Recombinant Proteins--analysis--AN; Recombinant Proteins --immunology--IM; Sensitivity and Specificity; Somatotropin--immunology--IM
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (H19 RNA); 0 (Muscle Proteins); 0 (Recombinant Proteins); 9002-72-6 (Somatotropin)
Record Date Created: 19960711

8/9/9
DIALOG(R)File 155:MEDLINE(R)

08738178 96089539 PMID: 8563133
Biological and immunochemical characterization of recombinant human thyrotrophin.
Canonne C; Papandreou M J; Medri G; Verrier B; Ronin C
Laboratoire d'Immunochimie des Hormones Glycoproteiques and U 270 INSERM, Faculte de Medecine Nord, Marseille, France.
Glycobiology (ENGLAND) Jul 1995, 5 (5) p473-81, ISSN 0959-6658 Journal Code: 9104124
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Recombinant human thyroid-stimulating **hormone** (recTSH) has recently been engineered to detect metastatic lesions in patients operated on for thyroid cancer. In this report, we have compared the microheterogeneity, carbohydrate (CHO) content, mitogenic potency and immunoreactivity of the biotechnology product to those of human **TSH** of pituitary origin (pitTSH). Compositional analysis revealed that recombinant (rec) **TSH** produced in Chinese hamster ovary cells was overglycosylated compared with the native **hormone** (21 and 14%, respectively) with a higher amount of sialic acid and lack of N-acetylgalactosamine. Electrofocusing followed by immunoblotting resolved recTSH into six **glycoforms** with pIs ranging from 6.0 to 8.6, which were converted to a major species of pI 8.9 by sialidase treatment. pitTSH contained five main **isoforms** of pI 6.5-8.2 distinct from those of recTSH and partially resistant to sialidase. Binding activity of both human TSHs to porcine thyroid membrane receptors was found to be similar, but recTSH appeared to be 20% active compared to pitTSH in eliciting cAMP production and cell growth in rat FRTL-5 cells. Immunoreactivity of the recombinant **hormone** was investigated using polyclonal and **monoclonal** antibodies raised against the native **hormone** or synthetic peptide sequences of its subunits. While rec- and pitTSH were recognized to a similar extent by anti-protein antibodies, they exhibited a different binding pattern to antipeptide antibodies. Serial dilution of anti-alpha 1-25, anti-alpha 26-51, anti-beta 96-112 antisera bound recTSH to a greater extent than pitTSH, while anti-beta 31-51 and anti-beta 53-76 displayed similar recognition toward both preparations. (ABSTRACT TRUNCATED AT 250 WORDS)
Tags: Animal; Human; Support, Non-U.S. Gov't
Descriptors: *Thyrotropin--chemistry--CH; Antibodies, **Monoclonal** --metabolism--ME; Binding, Competitive; CHO Cells--metabolism--ME; Carbohydrates--metabolism--ME; Cell Division--drug effects--DE; Electrophoresis, Polyacrylamide Gel; Enzyme-Linked Immunosorbent Assay; Epitopes--metabolism--ME; Glycosylation; Hamsters; Immunochemistry; Neuraminidase--pharmacology--PD; Pituitary Gland--metabolism--ME; Protein Engineering; Rats; Receptors, Thyrotropin--metabolism--ME; Recombinant Proteins--chemistry--CH; Recombinant Proteins--drug effects--DE; Recombinant Proteins--genetics--GE; Recombinant Proteins--immunology--IM; Recombinant Proteins--metabolism--ME; Swine; Thyrotropin--drug effects--DE ; Thyrotropin--genetics--GE; Thyrotropin--immunology--IM; Thyrotropin --metabolism--ME
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Carbohydrates); 0 (Epitopes); 0 (Receptors, Thyrotropin); 0 (Recombinant Proteins); 9002-71-5 (Thyrotropin)
Enzyme No.: EC 3.2.1.18 (Neuraminidase)

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S7      81799   S3 OR S4
S8     120261   E3-E50
S9     116146   R1-R7
S10       282   E1-E50
S11         4   E2-E3
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S15        50   TARGET - S14
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Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

To evaluate the presence of different GH isoforms in serum of girls with Turner's syndrome, we measured the serum GH content using RIAs with three different site-specific **monoclonal** antibodies (MAbs). We compared the results to those obtained with authentic GH and GH isoforms. Compared to pituitary GH (mol wt, 22K daltons) as the standard for all three MAbs, serum from girls with Turner's syndrome did not displace tracer [125I]GH equally with all three MAbs. The relative amounts of GH-immunoreactive material found in Turner's syndrome were different from the amounts observed in normal adults and most children with idiopathic short stature. The presence of GH, other than 22K GH, in serum from girls with Turner's syndrome was confirmed by affinity chromatography. The existence of different isoforms of GH, as shown by different cross-reactivity patterns with different MAbs to GH, may explain the conflicting results reported for GH secretion in girls with Turner's syndrome.

Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Somatotropin--blood--BL; *Turner Syndrome--blood--BL; Adolescence; Adult; Antibodies, **Monoclonal** ; Blood Specimen Collection; Child; Child, Preschool; Chromatography, Affinity; Clonidine--diagnostic use--DU; Cross Reactions; Growth Disorders--blood--BL; Levodopa--diagnostic use--DU; Pituitary Gland; Radioimmunoassay; Reference Values; Sex Characteristics; Somatotropin--analysis--AN; Somatotropin--secretion--SE

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Levodopa); 4205-90-7 (Clonidine); 9002-72-6 (Somatotropin)

Record Date Created: 19940705

8/9/23

DIALOG(R)File 155:MEDLINE(R)

07815185 93346545 PMID: 7688376

Variants of human chorionic gonadotropin from pregnant women and tumor patients recognized by monoclonal **antibodies.**

Berger P; Schwarz S; Spottl G; Wick G; Mann K

Institute for Biomedical Aging Research, Austrian Academy of Sciences, Innsbruck.

Journal of clinical endocrinology and metabolism (UNITED STATES) Aug 1993, 77 (2) p347-51, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

In biological fluids, hCG and its free alpha- (hCG alpha) and beta-subunits (hCG beta), occur in multiple forms. These various forms differ at the molecular level primarily in glycosylation, but also differ in protein backbone modifications corresponding to the urinary low molecular weight fragment of the hCG beta-subunit (beta-core fragment). This microheterogeneous nature can be demonstrated by isoelectric focusing in which variants are separated into bands with different isoelectric points (pI). To determine whether such isoelectric variants differ in antigenicity and consequently might escape immunoassay detection due to overspecificity of **monoclonal** antibodies (MCA), urinary pregnancy hCG (NIH, CR123) and tumor hCG preparations, such as a tumor-specific acidic variant of **hCG** (hCGav) and the **hCG** beta-core fragment, were separated by isoelectric focusing in the absence or presence of 8 M urea, or by sodium docedyl sulfate-polyacrylamide gel electrophoresis and enzymatically immunostained using an MCA panel directed against 17 different **hCG** epitopes. MCA against 14 different epitopes accessible on holo- **hCG** recognized all pI variants of pregnancy holo- **hCG** or tumor-derived hCGav, as was true for the three MCA recognizing epitopes hidden on holo- **hCG** but accessible on the free subunits after **hCG** dissociation by urea. We conclude that each individual pI- **isoform** of holo- **hCG** and its free subunits expresses the entire set of epitopes recognized by our MCA panel. The carbohydrate moieties that form a biochemical basis for **hCG**

heterogeneity seem to be neither of major antigenic relevance, nor are they structurally related to any particular epitope. Thus, various glycosylation forms of **hCG** , **hCG** alpha, **hCG** beta, and **hCG** beta-core in normal as well as in pathological samples should safely be detectable and measureable by immunoassays employing MCA with appropriate subunit specificity.

Tags: Female; Human; Male; Pregnancy

Descriptors: Antibodies, **Monoclonal** --immunology--IM; *Gonadotropins, Chorionic--immunology--IM; *Testicular Neoplasms--metabolism--ME; Antibodies, **Monoclonal** --diagnostic use--DU; Blotting, Western; Electrophoresis, Polyacrylamide Gel; Epitopes--immunology--IM; Gonadotropins, Chorionic --analysis--AN; Gonadotropins, Chorionic--isolation and purification--IP; Isoelectric Focusing; Testicular Neoplasms--chemistry--CH

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Gonadotropins, Chorionic)

Record Date Created: 19930909

8/9/26

DIALOG(R)File 155:MEDLINE(R)

07771907 93322032 PMID: 1306849

Prolactin isoforms secreted by human prolactinomas.

Hoffmann T; Gunz G; Brue T; Jaquet P; Ronin C

Laboratoire de Neuroendocrinologie Experimentale, INSERM U 297, Marseille, France.

Hormone research (SWITZERLAND) 1992, 38 (3-4) p164-70, ISSN 0301-0163 Journal Code: 0366126

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Prolactin (hPRL) secreted by human prolactinoma cells in culture was purified by gel filtration, lectin affinity chromatography and gel electrophoresis in order to identify the different **isoforms** of the **hormone** and to test their respective immunoreactivities and bioactivities. The nonglycosylated hPRL (NG-hPRL), unbound to lectins, was the major form and was a species (NG1-hPRL), of 23,000 (M(r)) apparent molecular weight. The lectin-bound glycosylated hPRL (G-hPRL) consisted of three forms, G1-, G2- and G3-hPRL, of identical molecular weights (25,000 M(r)). Endoglycosidase treatment indicated that these three forms differed by the heterogeneity of their carbohydrate chains. These G-PRLs proved to be 68% less immunoreactive and 50% less bioactive than NG-hPRL. It is concluded from these data that, in prolactinomas, the main variant of the hormone is the nonglycosylated form of PRL.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Pituitary Neoplasms--secretion--SE; *Prolactin--secretion --SE; *Prolactinoma--secretion--SE; Antibodies, **Monoclonal** ; Cell Division --drug effects--DE; Chromatography, Affinity; Chromatography, Gel; Electrophoresis, Polyacrylamide Gel; Glucosaminidase--metabolism--ME; Glycosylation; Immunoblotting; Immunoradiometric Assay; Isoelectric Focusing; Lymphoma; Molecular Weight; Prolactin--isolation and purification --IP; Prolactin--pharmacology--PD; Tumor Cells, Cultured

CAS Registry No.: 0 (Antibodies, Monoclonal); 9002-62-4 (Prolactin)

Enzyme No.: EC 3.2.1.- (Glucosaminidase)

Record Date Created: 19930816

8/9/28

DIALOG(R)File 155:MEDLINE(R)

07697258 93221365 PMID: 8466399

Review of the influence of polypeptide hormone forms on immunoassay results.

Howanitz J H

Laboratory Service, West Los Angeles Department of Veterans Affairs Medical Center, Calif.

Archives of pathology & laboratory medicine (UNITED STATES) Apr 1993, 117 (4) p369-72, ISSN 0003-9985 Journal Code: 7607091

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

Various forms of the polypeptide **hormones** that occur in blood, fluids, or tissues can differ according to physiologic and pathologic states. Forms include subunits of luteinizing **hormone** , follicle-stimulating **hormone** , human chorionic **gonadotropin** , and thyroid-stimulating **hormone** . Hormonal **isoforms** occur for these **hormones** as well as for prolactin and growth **hormone** . Variation in hormonal forms appears to contribute significantly to the wide variation in immunoassay results for these polypeptide **hormones** . Subunits and **isoforms** of the polypeptide **hormones** can overreact or underreact in **monoclonal** antibody assays. The underreaction or overreaction can occur with standards, controls, and patient specimens as well as with the assay label. (22 Refs.)

Tags: Human

Descriptors: *Gonadotropins--analysis--AN; *Immunoassay--standards--ST; *Neuropeptides--analysis--AN; Antibodies, **Monoclonal** ; Quality Control; Reference Standards; Reproducibility of Results

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Gonadotropins); 0 (Neuropeptides)

Record Date Created: 19930503

8/9/30
DIALOG(R)File 155:MEDLINE(R)

07608002 93142970 PMID: 1489087

Application of an immune-tolerizing procedure to generate monoclonal **antibodies specific to an alternate protein** isoform **of bovine growth** hormone .

Salata R A; Malhotra I J; Hampson R K; Ayers D F; Tomich C S; Rottman F M
Department of Medicine, Case Western Reserve University, School of Medicine, Cleveland, Ohio.

Analytical biochemistry (UNITED STATES) Nov 15 1992, 207 (1) p142-9, ISSN 0003-2697 Journal Code: 0370535

Contract/Grant No.: AI-15351; AI; NIAID; DK-32770; DK; NIDDK

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

An immune-tolerizing protocol was employed to generate **monoclonal** antibodies to a variant protein **isoform** of bovine growth **hormone** arising from alternative pre-mRNA processing. Variant bovine growth **hormone** used for immunization was obtained by expression in bacteria and electroelution of the protein from preparative sodium dodecyl sulfate-polyacrylamide gels. Balb/c mice were first immunized with wild-type bovine growth **hormone** in the presence of the cytotoxic drug cyclophosphamide, thereby tolerizing the mouse to common epitopes shared among the two proteins. Subsequently, the mice were immunized with variant bovine growth **hormone** to produce antibodies specific to variant epitopes. Comparisons of fusions resulting from standard and tolerizing immunization protocols resulted in a significantly enhanced production of variant bovine growth hormone-specific antibodies as a result of the immunotolerizing protocol. The specificity of the antibodies to the variant growth **hormone** was substantiated by differential enzyme-linked immunosorbent assay and Western blot. Nearly all **hybridomas** positive for variant growth **hormone** were negative for wild-type growth **hormone** . Finally, the antibodies were used to demonstrate intracytoplasmic staining of COS I cells transiently transfected with a variant growth **hormone** -producing plasmid. Given the power of the polymerase chain reaction to conveniently clone alternatively processed mRNA species, followed by expression in bacteria to provide antigen, the immunotolerizing protocol provides a convenient general method for producing antibodies specific to desired protein **isoforms** .

Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: Antibodies, **Monoclonal** --biosynthesis--BI; *Immune Tolerance; *Somatotropin--immunology--IM; Amino Acid Sequence; Antibodies,

Monoclonal --immunology--IM; Antibody Specificity; Cattle; Cells, Cultured ; Enzyme-Linked Immunosorbent Assay; Haplorhini; Immunization; Immunoblotting; Mice; Mice, Inbred BALB C; Molecular Sequence Data; Plasmids; Protein Processing, Post-Translational; RNA Precursors--genetics --GE; RNA, Messenger--genetics--GE; Somatotropin--genetics--GE; Somatotropin--metabolism--ME; Spleen--cytology--CY; Spleen--immunology --IM; Transfection; Variation (Genetics)

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Plasmids); 0 (RNA Precursors); 0 (RNA, Messenger); 9002-72-6 (Somatotropin)

Record Date Created: 19930224

8/9/36

DIALOG(R)File 155:MEDLINE(R)

07274994 92202070 PMID: 1551801

Is an immunoassay available for the measurement of bioactive LH in serum?

Rosenfield R L; Helke J

Department of Pediatrics, University of Chicago, Pritzker School of Medicine, Wyler Children's Hospital, Illinois 60637-1470.

Journal of andrology (UNITED STATES) Jan-Feb 1992, 13 (1) p1-10, ISSN 0196-3635 Journal Code: 8106453

Contract/Grant No.: HD-06308; HD; NICHD; RR-00055; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

An in vitro bioassay for luteinizing hormone (LH) is in our opinion the "gold standard" bioassay. The rodent interstitial cell testosterone assay (RICT) is specific for bioactive LH and very sensitive, accurate, and reproducible. Diverse LH standards consistently display parallel dose-response characteristics. Sera also manifest parallel dose-response characteristics throughout reproductive life, with the exception of basal samples from prepubertal children. This indicates that all known hormones with LH bioactivity have a similar bioactive site. The in vivo bioassays for **LH** used for calibration of World Health Organization standards are more cumbersome and less precise and accurate than the in vitro bioassay. The ovarian ascorbic acid depletion assay corresponds better than the seminal vesicle weight assay with in vitro bioassay. Variation in the ratio of bioactive to immunoreactive **LH** (B/I) principally reflects variation in **LH** immunoassay dose-response characteristics, rather than a change in the bioactive moiety of **LH** . The varying B/I ratio is due to molecular heterogeneity at multiple levels. Different **LH** standards contain different proportions of nonbioactive but immunoreactive material. The immunoreactive **LH** **isoforms** in serum contain different proportions of bioactive material and the **isoform** distribution differs with reproductive status. Furthermore, the antibodies comprising the various immunoassay systems detect heterogeneous epitopes on **LH** , which are not necessarily bioactive. B/I ratio disparities indicate lack of specificity of immunoassays for bioactive **LH** . Polyclonal antibody-based radioimmunoassay requires the use of purified reagents, including a bioactive tracer, in order to achieve high specificity for bioactive **LH** . The new generation of **monoclonal** antibody-based immunometric assays yields results that are lower than, but correlate with, **LH** measured by the in vitro bioassay. The purest of standards, even a recombinant standard, yields results that differ up to 50% or more from one immunoassay to another. Serum **LH** levels also differ up to two-fold among assays. The immunometric assays have the advantage of being more sensitive and more specific for low levels of **LH** in serum than radioimmunoassays, but B/I ratio discrepancies remain great. An immunoassay specific for the bioactive "docking site" of human **LH** **isoforms** is still needed.

Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.

Descriptors: *Immunoassay--methods--MT; *LH--blood--BL; Antibodies --immunology--IM; Immunoassay--trends--TD; LH--immunology--IM; Radioimmunoassay--methods--MT

CAS Registry No.: 0 (Antibodies); 9002-67-9 (LH)

Record Date Created: 19920428

?ds

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Set     Items   Description
S1       2541   (ISOFORM? OR GLYCOFORM?) (100N) (FSH OR HCG OR HORMONE? OR
            GONADOTRO? OR ESTROGEN? OR ESTRADIOL? OR HLH OR LH OR HFSH? OR
             TSH OR HTSH?)
S2        845   S1/2000:2002
S3       1696   S1 NOT S2
S4         95   S3 AND (MOAB OR MAB OR MONOCLONAL? OR HYBRIDOM?)
S5          5   S4 AND (MENOPAUS? OR PREMENOPAUS? OR POSTMENOPAUS?)
S6         90   S4 NOT S5
S7         39   TARGET - S6
S8         51   S6 NOT S7
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       14sep02 16:13:09 User228206 Session D1856.4
            $0.89    0.279 DialUnits File155
               $2.10  10 Type(s) in Format  9
            $2.10  10 Types
     $2.99  Estimated cost File155
     $0.21  TELNET
     $3.20  Estimated cost this search
     $3.20  Estimated total session cost   0.279 DialUnits


### Status: Signed Off. (1 minutes)
```

Pituitary glycoprotein hormone a-subunit secretion by cirrhotic patients.
Oliveira M C; Pizarro C B; Cassal A; Cremonese R; Vieira J G
Departamento de Endocrinologia, Fundacao Faculdade Federal de Ciencias Medicas de Porto Alegre, RS, Brasil. mco@portoweb.com.br
Brazilian journal of medical and biological research = Revista brasileira de pesquisas medicas e biologicas / Sociedade Brasileira de Biofisica ... et al (BRAZIL) Jan 1999, 32 (1) p73-7, ISSN 0100-879X
Journal Code: 8112917
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Secretion of the alpha-subunit of pituitary glycoprotein hormones usually follows the secretion of intact gonadotropins and is increased in gonadal failure and decreased in isolated gonadotropin deficiency. The aim of the present study was to determine the levels of the alpha-subunit in the serum of patients with cirrhosis of the liver and to compare the results obtained for eugonadal cirrhotic patients with those obtained for cirrhotic patients with hypogonadotropic hypogonadism. Forty-seven of 63 patients with cirrhosis (74.6%) presented hypogonadism (which was central in 45 cases and primary in 2), 7 were eugonadal, and 9 women were in normal **menopause** . The serum alpha-subunit was measured by the fluorimetric method using **monoclonal** antibodies. Cross-reactivity with LH, TSH, **FSH** and hCG was 6.5, 1.2, 4.3 and 1.1%, respectively, with an intra-assay coefficient of variation (CV) of less than 5% and an interassay CV of 5%, and sensitivity limit of 4 ng/l. The serum alpha-subunit concentration ranged from 36 to 6253 ng/l, with a median of 273 ng/l. The median was 251 ng/l for patients with central hypogonadism and 198 ng/l for eugonadal patients. The correlation between the alpha-subunit and basal LH levels was significant both in the total sample ($r = 0.48$, $P < 0.01$) and in the cirrhotic patients with central hypogonadism ($r = 0.33$, $P = 0.02$). Among men with central hypogonadism there was a negative correlation between alpha-subunit levels and total testosterone levels ($r = -0.54$, $P < 0.01$) as well as free testosterone levels ($r = -0.53$, $P < 0.01$). In conclusion, although the alpha-subunit levels are correlated with LH levels, at present they cannot be used as markers for hypogonadism in patients with cirrhosis of the liver.

Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Descriptors: *Glycoprotein Hormones, alpha Subunit--blood--BL; *Hypogonadism--blood--BL; *Liver Cirrhosis--blood--BL; Adult; Aged; Hypogonadism--diagnosis--DI; LH--blood--BL; Middle Age; Severity of Illness Index; Testosterone--blood--BL
CAS Registry No.: 0 (Glycoprotein Hormones, alpha Subunit); 57-85-2 (Testosterone); 9002-67-9 (LH)
Record Date Created: 19990909

16/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09012142 96379946 PMID: 8787959
Undetectable luteinizing hormone levels using a monoclonal **immunometric assay.**
Barbe F; Legagneur H; Watrin V; Klein M; Badonnel Y
Service de Biologie Medicale, Maternite Regionale, Nancy, France.
Journal of endocrinological investigation (ITALY) Nov 1995, 18 (10) p806-8, ISSN 0391-4097 Journal Code: 7806594
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Previous studies have shown wide discrepancies among the results obtained with different immunometric assays. We present five cases (out of 4000 women) whose plasma luteinizing hormone was not detected using a LH immunometric assay (LH Stratus Baxter) but was recognized by other kits. These cases concerned one 28-year-old woman presenting with infertility and four postmenopausal women. The LH Amerlite kit gave detectable but low

results. The results obtained with the other kits were > 7 IU/l. **FSH** levels were > 7 IU/l. In one case, sera were taken before and after the **menopause** ; differences between the LH results increased. Discrepancies among LH assay kits have been attributed to variation both in standard curve calibration and in epitope specificity of the kit **monoclonal** antibodies. The Baxter kit might misrecognize some isoforms present in postmenopausal women. The present data illustrate the potential false results with such immunoassays in routine clinical laboratory testing. When undetectable LH results are not clinically explained or when disparities between LH and **FSH** are observed, we suggest using a second methodology or a bioassay if necessary. Improvement in LH assays and standardization might resolve the problem of discrepancies between the LH results.

Tags: Comparative Study; Female; Human

Descriptors: Antibodies, **Monoclonal** ; *Immunoassay--methods--MT; *LH --blood--BL; Adult; False Negative Reactions; **Follicle Stimulating Hormone** --blood--BL; Immunoassay--statistics and numerical data--SN; Middle Age; **Postmenopause** ; Reagent Kits, Diagnostic--statistics and numerical data --SN

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)

Record Date Created: 19961021

16/9/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07454398 92388366 PMID: 1517372

Differing responses of plasma bioactive and immunoreactive follicle-stimulating hormone and luteinizing hormone to gonadotropin-releasing hormone antagonist and agonist treatments in postmenopausal women.

Matikainen T; Ding Y Q; Vergara M; Huhtaniemi I; Couzinet B; Schaison G

Department of Physiology, University of Turku, Finland.

Journal of clinical endocrinology and metabolism (UNITED STATES) Sep 1992, 75 (3) p820-5, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Plasma bioactive (B) and immunoreactive (I) **FSH** and LH were measured every 10 min for 8 h in the same postmenopausal women in a three-phase study: 1) during normal pulsatile gonadotropin secretion (basal study; n = 8), 2) 8 h after a single injection of a GnRH antagonist (5 mg Nal-Glu, sc; n = 5), and 3) 21 days after a GnRH agonist injection (D-Trp6, 3.75 mg depot preparation, im; n = 7). I- **FSH** and I-LH were measured by **monoclonal** antibody immunoradiometric assays. B- **FSH** and B-LH were measured in selected samples with the immature rat granulosa cell and mouse interstitial cell assays, respectively. Significant pulsatility of B- and I- **FSH** and LH was demonstrated in the basal samples, but only the B/I ratio of LH was slightly elevated within the secretion peaks. After GnRH antagonist treatment, I- **FSH** decreased from a mean pretreatment level of 55.7 +/- 7.8 IU/L by 26% (P less than 0.001), and B- **FSH** from 313.8 +/- 61.9 IU/L by 44% (P less than 0.01). The B/I ratio decreased from 6.4 +/- 1.7 to 4.5 +/- 1.0 (P less than 0.05). After agonist treatment, the I- and B- **FSH** levels decreased by 92% and 83% (P less than 0.0001), respectively, but the B/I ratio increased to 17.3 +/- 4.7 (P less than 0.05). The concentrations of I- and B-LH decreased by 75% and 80%, respectively (P less than 0.001), after antagonist treatment. After agonist treatment, I-LH decreased by 92%, and B-LH by 93% (P less than 0.0001). No changes in the B/I ratios of LH were found after either treatment. In conclusion, no changes were found in the quality of circulating LH during the treatments, whereas the antagonist treatment decreased and the agonist treatment increased the B/I ratio of **FSH** . These findings provide further evidence that the qualitative responses of **FSH** and LH to treatment with the same GnRH analog are different, and that the suppressive mechanisms of GnRH antagonist and agonist action on gonadotropin secretion are different.

Tags: Comparative Study; Female; Human; Support, Non-U.S. Gov't

Descriptors: **Follicle Stimulating Hormone** --blood--BL; *Gonadorelin

Salt Lake City 84132.
Journal of clinical endocrinology and metabolism (UNITED STATES) Jul 1989, 69 (1) p170-6, ISSN 0021-972X Journal Code: 0375362
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

hCG has biological properties similar to those of LH, but can be measured separately from LH by current radioimmunometric assays. To investigate the possible existence of an autoregulatory mechanism for LH in humans, we compared the basal LH concentrations and the LH response to a GnRH stimulus with and without prior administration of hCG. On two separate occasions, at least 1 week apart, six normal (eugonadal) males and six normal postmenopausal females were given, in random order, either 10,000 IU hCG or saline followed by iv injection of a 200-micrograms bolus of GnRH. Blood samples were then taken 30, 60, 90, 120, 180, 240, and 300 min after GnRH. Serum concentrations of LH and hCG were measured at each time by two **monoclonal** antibody sandwich assays developed in our laboratory. After exogenous hCG, serum hCG concentrations rose rapidly to 200-500 IU/L (15,000-35,000 pg/mL) in both the men and women, remaining at this high level throughout the study. In the men, sex steroid concentrations did not change in response to the hCG during the 9 study hours. Compared to saline-treated controls, hCG had no significant effect in either men or postmenopausal women on the basal LH concentration or the response to a GnRH bolus, as determined by peak response and area under the LH/time curve between 0-300 min after GnRH. We conclude that an ultrashort loop feedback mechanism for LH on its own secretion does not exist in humans, as assessed by the present protocol.

Tags: Comparative Study; Female; Human; Male
Descriptors: *Gonadorelin--administration and dosage--AD; *Gonadotropins, Chorionic--administration and dosage--AD; *Gonadotropins, Chorionic --pharmacology--PD; *LH--blood--BL; Adult; Binding Sites; Estradiol--blood --BL; Feedback--drug effects--DE; **Follicle Stimulating Hormone** --blood--BL ; Gonadorelin--pharmacology--PD; LH--secretion--SE; **Menopause** ; Middle Age ; Pituitary Gland--drug effects--DE; Pituitary Gland--secretion--SE; Receptors, LH--blood--BL; Testosterone--blood--BL
CAS Registry No.: 0 (Gonadotropins, Chorionic); 0 (Receptors, LH); 33515-09-2 (Gonadorelin); 50-28-2 (Estradiol); 57-85-2 (Testosterone) ; 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19890719

16/9/6 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07601914 EMBASE No: 1999100685
Postmenopause is associated with a decrease in serum inhibin A and inhibin B levels but not in activin A
Pezzani I.; Luisi S.; Santuz M.; Florio P.; Plaino L.; Fadalti M.; Fabiani G.; Driul P.G.; Genazzani A.R.; Petraglia F.
Italian Journal of Gynaecology and Obstetrics (ITAL. J. GYNAECOL. OBSTET.) (Italy) 1998, 10/3 (83-86)
CODEN: IJGOE ISSN: 1121-8339
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 17

Objective: The aim of the present study was to evaluate the changes in serum inhibin A, inhibin B and activin A levels in **postmenopause** . Methods: Specific assays for inhibin A, inhibin B and activin A were used and two groups of women were studied: 1) postmenopausal (n = 55) (aged 48-59 years), with a subgroup of 18 surgical menopause; 2) fertile healthy women (n = 50) (aged 19-35 years). The assays for inhibin A, inhibin B and activin A were two-site enzime immunoassay based on the use of plates coated with specific **monoclonal** antibodies; serum **FSH** , LH, 17beta-estradiol levels were determined by radioimmunoassay. Results: Mean

+/- SEM serum inhibin A and inhibin B levels in postmenopausal women were significantly lower than in fertile women ($p < 0.01$). The decreased levels of both inhibins were independent of the length or the type of menopause (natural or surgical). No significant difference of activin A levels was observed between postmenopausal and fertile women. Conclusion: The present study showed that both inhibin A and inhibin B levels decrease in postmenopausal women independently of age, length and form of menopause and they may represent a distinctive marker of ovarian failure. No changes of activin A levels has been observed after menopause suggesting that ovary is not the major source for circulating activin A.

DRUG DESCRIPTORS:
*inhibin a--endogenous compound--ec; *activin a--endogenous compound--ec
monoclonal antibody; **follitropin** --endogenous compound--ec; luteinizing hormone--endogenous compound--ec; estradiol--endogenous compound--ec
MEDICAL DESCRIPTORS:
* **postmenopause** --etiology--et
hormone blood level; blood analysis; **premenopause** --etiology--et; enzyme immunoassay; radioimmunoassay; **follitropin** blood level; luteinizing hormone blood level; estradiol blood level; comparative study; age; ovary function; human; female; major clinical study; adult; article
CAS REGISTRY NO.: 104625-48-1 (activin a); 9002-68-0 (**follitropin**); 39341-83-8, 9002-67-9 (luteinizing hormone); 50-28-2 (estradiol
SECTION HEADINGS:
003 Endocrinology
010 Obstetrics and Gynecology
029 Clinical and Experimental Biochemistry

16/9/7 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05519479 EMBASE No: 1993287578
Effects of oophorectomy and hormone replacement therapy on pituitary-gonadal function
Castelo-Branco C.; Martinez de Osaba M.J.; Vanrezc J.A.; Fortuny A.; Gonzalez-Merlo J.
Department of Gynecology/Obstetrics, Hospital Clinic i Provincial, c/Villarroel 170,08036 Barcelona Spain
Maturitas (MATURITAS) (Ireland) 1993, 17/2 (101-111)
CODEN: MATUD ISSN: 0378-5122
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The purpose of this study was to determine how oophorectomy and different hormone replacement therapy (HRT) regimens using low doses of medroxyprogesterone acetate (MPA, 2.5 mg/day) influence the pituitary-gonadal axis function. Ninety (90) women, who had had regular menses prior to surgery, completed a 1-year follow-up period. Patients were assigned to 5 groups. The first (n = 16) received 0.625 mg/day conjugated equine oestrogens (CEE) cyclically, the second (n = 20) 50 mug/day transdermal oestradiol (Einf 2) cyclically and the third (n = 15) 0.625 mg/day CEE continuously. These 3 groups also received 2.5 mg MPA sequentially for the last 12 days of HRT administration. The fourth group (n = 20) received 0.625 mg/day CEE and 2.5 mg/day of MPA continuously, while the fifth (n = 19) constituted a control group. After oophorectomy all patients showed increases in follicle-stimulating hormone (**FSH**) and luteinizing hormone (LH) levels, and decreases in those of Einf 2, oestrone (Einf 1), prolactin (PRL), sex-hormone-binding globulin (SHBG), androstenedione (DeltaAinf 4) and testosterone (T). No changes were detected in dehydroepiandrosterone sulphate (DHEA-S) levels. After HRT, decreases in **FSH** , LH and PRL levels and increases in those of Einf 2, Einf 1 and SHBG were observed, but no changes were seen in T, DeltaAinf 4 or DHEA-S plasma levels. As the differences that were found cannot be attributed to the presence of ovaries, it is reasonable to assume that they were perhaps due to the treatment. All these changes, with the exception of a decrease in PRL levels, are therefore to be expected after HRT.

DRUG DESCRIPTORS:
*estrogen--pharmacology--pd; * **follitropin** --endogenous compound--ec; * luteinizing hormone--endogenous compound--ec; *medroxyprogesterone acetate --pharmacology--pd; *prolactin--endogenous compound--ec androstenedione--endogenous compound--ec; **monoclonal** antibody; testosterone--endogenous compound--ec
MEDICAL DESCRIPTORS:
*hormonal therapy; *hypophysis; *menopause; *ovariectomy adult; article; controlled study; drug effect; female; human; major clinical study; priority journal; transdermal drug administration
CAS REGISTRY NO.: 9002-68-0 (**follitropin**); 39341-83-8, 9002-67-9 (luteinizing hormone); 71-58-9 (medroxyprogesterone acetate); 12585-34-1 , 50647-00-2, 9002-62-4 (prolactin); 26264-53-9, 63-05-8 (androstenedione); 58-22-0 (testosterone
SECTION HEADINGS:
003 Endocrinology
009 Surgery
010 Obstetrics and Gynecology
020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

16/9/9 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01855508 91168376 PMID: 1900742
Interpretations of five monoclonal **immunoassays of lutropin and follitropin: effects of normalization with WHO standard.**
Vermes I; Bonte H A; v d Sluijs Veer G; Schoemaker J
Department of Clinical Chemistry, Medisch Spectrum Twente, Enschede, The Netherlands.
Clin Chem (UNITED STATES) Mar 1991, 37 (3) p415-21, ISSN 0009-9147 Journal Code: 9421549
Comment in Clin Chem. 1991 Mar;37(3) 311-2; Comment in PMID 2004435
Document Type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Five mono(oligo)clonal immunometric assays for lutropin (LH) and follitropin (**FSH**)--bioMerieux, IRE-Medgenix, Serono Diagnostics, Diagnostics Products Corp. (DPC), and LKB--were evaluated in comparison with two polyclonal RIAs (DPC and Amersham). Detection limits varied from 0.04 to 0.32 int. unit/L and 0.06 to 0.86 int. unit/L for LH and **FSH** , respectively. Intra- and interassay precision (CV) at three concentrations varied from 2.0% to 29.8%, showing that not all kits tested gave acceptable results, especially for LH. Linearity and parallelism were acceptable, except for the DPC **FSH** kit and the bioMerieux LH kit. High-dose "hook" effects were seen in some kits at LH concentrations of 250 int. units/L, but not in the **FSH** kits up to concentrations of 350 int. units/L. Reagents in some kits cross-reacted with choriogonadotropin. The clinical validity of the assays was tested in 25 pre- and 25 postmenopausal healthy women and in 66 patients with polycystic ovary disease. In contrast to **FSH** , LH values varied significantly not only between polyclonal and **monoclonal** assays but also between the various **monoclonal** assays, despite the fact that all manufacturers state that their kits are calibrated on the same standards: WHO International Reference Preparation (IRP) 68/40 for LH and 78/549 for **FSH** . We normalized the results by using new WHO standards: IRP 80/552 for LH and IRP 83/575 for **FSH** . This decreased significantly the between-kit differences in LH results for individuals. The much-used LH/ **FSH** ratio greater than 3 for diagnosing patients with polycystic ovary disease is not valid when **monoclonal** assays are used, and is kit-dependent. However, using the normalized results yields a "new" LH/ **FSH** ratio, which is kit-independent and differs significantly between patients and healthy subjects.
Tags: Comparative Study; Female; Human
Major Descriptors: **Follicle Stimulating Hormone** --blood--BL; *LH--blood

--BL; *Radioimmunoassay--methods--MT
Minor Descriptors: Adolescence; Adult; Immunoradiometric Assay--methods --MT; **Menopause** --blood--BL; Polycystic Ovary Syndrome--blood--BL; Reagent Kits, Diagnostic; Reference Standards
CAS Registry No.: 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19910424
?logoff hold
14sep02 16:38:25 User228206 Session D1856.10

Undetectable luteinizing hormone levels using a monoclonal **immunometric assay.**

Barbe F; Legagneur H; Watrin V; Klein M; Badonnel Y
Service de Biologie Medicale, Maternite Regionale, Nancy, France.

Journal of endocrinological investigation (ITALY) Nov 1995, 18 (10) p806-8, ISSN 0391-4097 Journal Code: 7806594
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Previous studies have shown wide discrepancies among the results obtained with different immunometric assays. We present five cases (out of 4000 women) whose plasma luteinizing hormone was not detected using a LH immunometric assay (LH Stratus Baxter) but was recognized by other kits. These cases concerned one 28-year-old woman presenting with infertility and four postmenopausal women. The LH Amerlite kit gave detectable but low results. The results obtained with the other kits were > 7 IU/l. **FSH** levels were > 7 IU/l. In one case, sera were taken before and after the **menopause** ; differences between the LH results increased. Discrepancies among LH assay kits have been attributed to variation both in standard curve calibration and in epitope specificity of the kit **monoclonal** antibodies. The Baxter kit might misrecognize some isoforms present in postmenopausal women. The present data illustrate the potential false results with such immunoassays in routine clinical laboratory testing. When undetectable LH results are not clinically explained or when disparities between LH and **FSH** are observed, we suggest using a second methodology or a bioassay if necessary. Improvement in LH assays and standardization might resolve the problem of discrepancies between the LH results.

Tags: Comparative Study; Female; Human
Descriptors: Antibodies, **Monoclonal** ; *Immunoassay--methods--MT; *LH --blood--BL; Adult; False Negative Reactions; **Follicle Stimulating Hormone** --blood--BL; Immunoassay--statistics and numerical data--SN; Middle Age; **Postmenopause** ; Reagent Kits, Diagnostic--statistics and numerical data --SN
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19961021

--antagonists and inhibitors--AI; *LH--blood--BL; * **Menopause** ; Adult; *Biological Assay; Gonadorelin--physiology--PH; Immunoradiometric Assay; Middle Age; Osmolar Concentration
CAS Registry No.: 33515-09-2 (Gonadorelin); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19921008

16/9/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06861453 91168376 PMID: 1900742
Interpretations of five monoclonal **immunoassays of lutropin and follitropin: effects of normalization with WHO standard.**
Vermes I; Bonte H A; v d Sluijs Veer G; Schoemaker J
Department of Clinical Chemistry, Medisch Spectrum Twente, Enschede, The Netherlands.
Clinical chemistry (UNITED STATES) Mar 1991, 37 (3) p415-21, ISSN 0009-9147 Journal Code: 9421549
Comment in Clin Chem. 1991 Mar;37(3) 311-2; Comment in PMID 2004435
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Five mono(oligo)clonal immunometric assays for lutropin (LH) and follitropin (**FSH**)--bioMerieux, IRE-Medgenix, Serono Diagnostics, Diagnostics Products Corp. (DPC), and LKB--were evaluated in comparison with two polyclonal RIAs (DPC and Amersham). Detection limits varied from 0.04 to 0.32 int. unit/L and 0.06 to 0.86 int. unit/L for LH and **FSH** , respectively. Intra- and interassay precision (CV) at three concentrations varied from 2.0% to 29.8%, showing that not all kits tested gave acceptable results, especially for LH. Linearity and parallelism were acceptable, except for the DPC **FSH** kit and the bioMerieux LH kit. High-dose "hook" effects were seen in some kits at LH concentrations of 250 int. units/L, but not in the **FSH** kits up to concentrations of 350 int. units/L. Reagents in some kits cross-reacted with choriogonadotropin. The clinical validity of the assays was tested in 25 pre- and 25 postmenopausal healthy women and in 66 patients with polycystic ovary disease. In contrast to **FSH** , LH values varied significantly not only between polyclonal and **monoclonal** assays but also between the various **monoclonal** assays, despite the fact that all manufacturers state that their kits are calibrated on the same standards: WHO International Reference Preparation (IRP) 68/40 for LH and 78/549 for **FSH** . We normalized the results by using new WHO standards: IRP 80/552 for LH and IRP 83/575 for **FSH** . This decreased significantly the between-kit differences in LH results for individuals. The much-used LH/ **FSH** ratio greater than 3 for diagnosing patients with polycystic ovary disease is not valid when **monoclonal** assays are used, and is kit-dependent. However, using the normalized results yields a "new" LH/ **FSH** ratio, which is kit-independent and differs significantly between patients and healthy subjects.
Tags: Comparative Study; Female; Human
Descriptors: **Follicle Stimulating Hormone** --blood--BL; *LH--blood--BL; *Radioimmunoassay--methods--MT; Adolescence; Adult; Immunoradiometric Assay --methods--MT; **Menopause** --blood--BL; Polycystic Ovary Syndrome--blood--BL ; Reagent Kits, Diagnostic; Reference Standards
CAS Registry No.: 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19910424

16/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06194421 89278281 PMID: 2499588
Inability to demonstrate an ultrashort loop feedback mechanism for luteinizing hormone in humans.
Kyle C V; Griffin J; Jarrett A; Odell W D
Department of Internal Medicine, University of Utah School of Medicine,

Undetectable luteinizing hormone levels using a monoclonal **immunometric assay.**

Barbe F; Legagneur H; Watrin V; Klein M; Badonnel Y
Service de Biologie Medicale, Maternite Regionale, Nancy, France.

Journal of endocrinological investigation (ITALY) Nov 1995, 18 (10) p806-8, ISSN 0391-4097 Journal Code: 7806594
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Previous studies have shown wide discrepancies among the results obtained with different immunometric assays. We present five cases (out of 4000 women) whose plasma luteinizing hormone was not detected using a **LH** immunometric assay (**LH** Stratus Baxter) but was recognized by other kits. These cases concerned one 28-year-old woman presenting with infertility and four **postmenopausal** women. The **LH** Amerlite kit gave detectable but low results. The results obtained with the other kits were > 7 IU/l. **FSH** levels were > 7 IU/l. In one case, sera were taken before and after the **menopause** ; differences between the **LH** results increased. Discrepancies among **LH** assay kits have been attributed to variation both in standard curve calibration and in epitope specificity of the kit **monoclonal** antibodies. The Baxter kit might misrecognize some **isoforms** present in **postmenopausal** women. The present data illustrate the potential false results with such immunoassays in routine clinical laboratory testing. When undetectable **LH** results are not clinically explained or when disparities between **LH** and **FSH** are observed, we suggest using a second methodology or a bioassay if necessary. Improvement in **LH** assays and standardization might resolve the problem of discrepancies between the **LH** results.

Tags: Comparative Study; Female; Human
Descriptors: Antibodies, **Monoclonal** ; *Immunoassay--methods--MT; *LH --blood--BL; Adult; False Negative Reactions; Follicle Stimulating Hormone --blood--BL; Immunoassay--statistics and numerical data--SN; Middle Age; **Postmenopause** ; Reagent Kits, Diagnostic--statistics and numerical data --SN
CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH); 9002-68-0 (Follicle Stimulating Hormone)
Record Date Created: 19961021

5/9/3
DIALOG(R)File 155:MEDLINE(R)

req 9/14/01

09150210 97046606 PMID: 8891527

Interest of epitopic dissection in immunoanalysis of proteins and peptides: review of theoretical and practical aspects.

Niccoli P; Ferrand V; Lejeune P J; Carayon P

Laboratoire de Biochimie Endocrinienne et Metabolique, Institut National de la Sante et de la Recherche Medicale, Faculte de Medecine, Marseille, France.

European journal of clinical chemistry and clinical biochemistry : journal of the Forum of European Clinical Chemistry Societies (GERMANY) Sep 1996, 34 (9) p741-8, ISSN 0939-4974 Journal Code: 9105775

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The literature abounds with reports showing discrepancies in immunoassays of proteins and peptides. Whereas the isomorphism and polymorphism of proteins remains largely hidden in immunoassays making use of polyclonal antibodies, the use of **monoclonal** antibodies uncovered the difficulty of accurately assaying microheterogeneous analytes. Indeed, most proteic **hormones** are not entities with unique structures but rather mixtures of molecular forms with slight differences in structure which may reflect large variations in biological and immunological activities; the **monoclonal** antibodies appeared clearly less suited than the polyclonal for testing a mixture of **isoforms** . Protein microheterogeneity also has an impact on assay standardisation, since reference preparations may contain several **isoforms** of the analyte. Using recombinant glycoprotein does not solve the problem. Regarding the problem of discrepancy in immunoanalysis of proteins and peptides, we could establish, in a previous work, that discrepancy among lutropin assay kits may be related to various causes: i) differences in standard preparation and calibration curves; ii) microheterogeneity of lutropin molecules leading to missing some isoforms due to the restricted epitopic specificity of the **monoclonal** antibodies used in the kits. The epitopic dissection we engaged in appeared thus instrumental in explaining these discrepancies. It allowed us to enumerate epitopes on the surface of lutropin molecules, to elucidate the immunological structure and, finally, to characterize **monoclonal** antibodies used in commercially available lutropin assay kits with regard to their epitopic specificity. This work allowed us to interpret the discrepancy in serum lutropin concentration which was related to the use of **monoclonal** antibody with given specificity. Epitopic dissection may thus be instrumental in explaining discrepancy among immunoassays of proteins and peptides and in improving the accuracy of kits. (19 Refs.)

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Epitopes--chemistry--CH; *Immunoassay--methods--MT; *Peptides--chemistry--CH; *Proteins--chemistry--CH; Antibodies, **Monoclonal** ; Kidney Failure--blood--BL; LH--blood--BL; **Menopause** --blood--BL; Polycystic Ovary Syndrome--blood--BL; Polymorphism (Genetics); Reagent Kits, Diagnostic--standards--ST; Reference Values

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Epitopes); 0 (Peptides); 0 (Proteins); 0 (Reagent Kits, Diagnostic); 9002-67-9 (LH)

Record Date Created: 19970206

Postmenopause **is associated with a decrease in serum inhibin A and inhibin B levels but not in activin A**

Pezzani I.; Luisi S.; Santuz M.; Florio P.; Plaino L.; Fadalti M.; Fabiani G.; Driul P.G.; Genazzani A.R.; Petraglia F.

Italian Journal of Gynaecology and Obstetrics (ITAL. J. GYNAECOL. OBSTET.) (Italy) 1998, 10/3 (83-86)
CODEN: IJGOE ISSN: 1121-8339
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 17

Objective: The aim of the present study was to evaluate the changes in serum inhibin A, inhibin B and activin A levels in **postmenopause** . Methods: Specific assays for inhibin A, inhibin B and activin A were used and two groups of women were studied: 1) postmenopausal (n = 55) (aged 48-59 years), with a subgroup of 18 surgical menopause; 2) fertile healthy women (n = 50) (aged 19-35 years). The assays for inhibin A, inhibin B and activin A were two-site enzime immunoassay based on the use of plates coated with specific **monoclonal** antibodies; serum **FSH** , LH, 17beta-estradiol levels were determined by radioimmunoassay. Results: Mean +/- SEM serum inhibin A and inhibin B levels in postmenopausal women were significantly lower than in fertile women ($p < 0.01$). The decreased levels of both inhibins were independent of the length or the type of menopause (natural or surgical). No significant difference of activin A levels was observed between postmenopausal and fertile women. Conclusion: The present study showed that both inhibin A and inhibin B levels decrease in postmenopausal women independently of age, length and form of menopause and they may represent a distinctive marker of ovarian failure. No changes of activin A levels has been observed after menopause suggesting that ovary is not the major source for circulating activin A.

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L3: Entry 8 of 15 File: USPT Jan 5, 1999

DOCUMENT-IDENTIFIER: US 5855905 A
TITLE: Compound preparation for the treatment of hypogonadal men and men with hypophyseal diseases

Brief Summary Text (18):
The advantages of estradiol at a low concentration are indispensable, though (as is the case when administering non-aromatizable dihydrotestosterone or one of its derivatives). These advantages include an improvement of cognitive performance, an increase in the level of sex hormone-binding globulin (SHBG), the inhibition of LDL cholesterol oxidation as an important step in atherogenesis, arterial dilatation and the associated improved blood flow through the tissue, and the inhibition of increased gonadotropin and inhibin levels (Harman SM. Blackman MR. (1994) Male menopause, myth or menace? Endocrinologist 4:212-217). Moreover, estradiol seems to prevent age-dependent transformation processes in proteohormones (Wide L. Maessen T. (1994) 17.beta.-Estradiol counteracts the formation of the more acidic isoforms of follicle-stimulating hormone and luteinizing hormone after menopause. Clin Endocronol 40: 783-789).

Other Reference Publication (21):
"17.beta.-Oestradiol counteracts the formation of the more acidic isoforms of follicle-stimulating hormone and luteinizing hormone after menopause," Leif Wide et al. Clinical Endocrinology, vol. 40, (1994) pp. 783-789.

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L3: Entry 6 of 15 File: USPT Apr 16, 2002

DOCUMENT-IDENTIFIER: US 6372493 B1
TITLE: Hormone-secreting cells maintained in long-term culture

Brief Summary Text (16):
There exists a need for methods to produce consistent physiologically correct preparations of gonadotrophin hormones. Human gonadotrophin preparations (hMG), which typically contain both FSH and LH, are administered to women who are undergoing pre-treatment leading to in vitro fertilization. The administered hMG stimulates the woman's ovaries to produce multiple pre-ovulatory follicles, which are subsequently aspirated for in vitro fertilization. hMG is currently derived from the urine of post-menopausal women. Each lot differs according to the age and endocrine status of the urine donors, the differences being in both concentration and types of isoforms present in the final product. There are at least 11 isoforms of human follicle-stimulating hormone (hFSH) and 7 isoforms of human luteinizing hormone (hLH) (Stone, B. A., et al. 1990 Acta Endo (Copenhagen) 123:161-168). Analysis by high-performance liquid chromatography (HPLC) of various hMG preparations showed between-lot variability in the presence and concentration of isoforms of FSH (Stone, B. A. et al, supra). Different isoforms have different biopotencies (Gharib, S. D., et al. 1990 In: Endocrine Reviews 11:177-199). Since certain isoforms of FSH are more biopotent than others, there is between-lot variability in biopotency among various hMG preparations. Moreover, the presence of LH isoforms in a preparation affects the biopotency of FSH present in the preparation.

Brief Summary Text (21):
There also exists a need for a source of physiologically correct preparations of human sex steroid hormones. Currently, therapeutic estrogen and progesterone compounds, and analogs thereof, are prepared by standardized chemical synthesis. However, the class of compounds designated "estrogens" produced normally in the human female includes several different formulae and isoforms. Similarly, the class of hormones designated "progestins" includes several different compounds and isoforms. The types and amounts of estrogens and progestins produced naturally vary according to the female's age and overall physiological status, i.e., the specific time point in her menstrual cycle, pregnancy, or menopause. The optimal steroid content for any given therapeutic indication has not been determined. Even if the optimal chemical profile of a sex steroid preparation were determined, chemical synthesis would not be a practical route for production of complex steroid mixtures. Therefore, it is desirable to develop methods which inherently provide a physiologically correct mix of human estrogens and progesterones.

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L3: Entry 2 of 15 File: PGPB May 30, 2002

DOCUMENT-IDENTIFIER: US 20020064501 A1
TITLE: Immunoregulator

Detail Description Paragraph (49):
[0128] hCG is a member of the structural superfamily of cysteine knot growth factors like NGF, PDGF-B and TGF-beta and a members of the glycoprotein hormone family which also includes LH, FSH and TSH. They each consist of two non-covalently associated protein subunits, a common 15 kd alpha chain and a hormone specific 23 kd beta chain (Ann. Rev. Biochem., 50:465-495). hCG is produced by placental trophoblasts of normal pregnancy, and in gestational trophoblastic disease. It is also produced in much smaller quantities by the pituitary (Endocrinology, 137:1402-1411) in both pre- and postmenopausal women and in men (Trends in Endocrinology and Metabolism, 1:418-421), in many non-gestational malignant tumors and other tissues. hCG possesses a complex structure as a family of isoforms with structural, immunological and biological differences. The chemical basis for this heterogeneity is not known with certainty but differences in the amino acid composition, carbohydrate residues or both have been proposed. More recently it was also shown that oxidation of specific methionine residues may also be responsible. Different forms of hCG, alpha and beta-subunits, their nicked fragments, beta-core fragment and multiple isoforms of hCG have been reported in different tissues and body fluids (Journal of Endocrinology, 161:99-106; Endocrinology, 129:1541-1550; Obstet. Gynecol, 77:53-59; Journal of Biochemistry, 107, 858-862; Obstet. Gynecol., 80:223-228; Endocrinology, 133:985-989(1993); Endocrinology, 129:1551-1558; Endocrinology, 130:2052-2058; Journal of Endocrinology, 135:175-188; Endocrinology, 139, 519-532; Molecular and Cellular Endocrinology, 125:93-131).